WHAT IS CLAIMED IS:

1. An opener or activator compound which modulates the biological activity of central nervous system-associated KCNQ potassium channel polypeptides by hyperpolarizing neurons that fire before or during a migraine headache or migraine-related disorder.

2. An opener or activator compound which modulates the biological activity of central nervous system-associated KCNQ potassium channel polypeptides by preventing abnormal synchronous neuronal firing associated with migraine or migraine-related disorders.

3. The opener or activator compound according to claim 1 or claim 2, said compound selected from the group consisting of fluorooxindole and 2,4-disubstituted pyrimidine-5-carboxamide derivative compounds.

4. The compound according to claim 3, wherein the opener or activator compound is (+)-3-[5-Chloro-2-[(2,2,2-trifluoroethoxy)phenyl]-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2*H*-indol-2-one or 2-(Pyrrolidin-1-yl)-4-(trifluoromethyl)-N-[[4-(trifluoromethyl) phenyl]methyl] pyrimidine-5-carboxamide.

5. The compound according to claim 1 or claim 2, wherein the KCNQ potassium channel polypeptide is selected from the group consisting of one or more of KCNQ2, KCNQ3, KCNQ4, KCNQ5, and heteromultimers thereof.

6. A method of modulating neuronal activity associated with migraine or a migraine-related disorder, comprising administering to an individual in need thereof an amount of the compound according to claim 1 or claim 2 effective to inhibit neuronal activity, thereby reducing, ameliorating or alleviating migraine or a migraine-related disorder.

7. The method according to claim 6, wherein said neuronal activity is selectively inhibited within the trigeminovascular system of the central nervous system.

8. A method of treating migraine or a migraine-related disorder, comprising: administering to an individual in need thereof an opener of a CNS-located KCNQ potassium channel protein, or functional portion thereof, according to claim 1 or claim 2, in an amount effective to selectively limit neuronal hyperexcitability during a migraine attack or migraine-related disorder by opening the CNS-located KCNQ potassium channel protein so as to protect against abnormal synchronous firing of neurons.

9. The method according to claim 8, wherein the neuronal hyperexcitability occurs within the trigeminovascular system of the central nervous system.

10. The method according to claim 6 or claim 8, wherein the KCNQ potassium channel protein is selected from the group consisting of human KCNQ2, KCNQ3, KCNQ4, KCNQ5 and heteromultimers thereof.

11. The method according to claim 6 or claim 8, wherein the CNS-located KCNQ potassium channel protein opener is a fluorooxindole compound or a 2,4-disubstituted pyrimidine-5-carboxamide derivative compound.

12. A method of identifying biological compounds for treating migraine or a migraine-related disorder, comprising:

a) providing a central nervous system-associated KCNQ potassium channel protein;

b) contacting the KCNQ potassium channel protein with a test biological compound;

c) identifying those test compounds that are openers or activators of the KCNQ potassium channel protein; and

d) determining whether the KCNQ potassium channel opener or activator test compound produces a reduction in superior sagittal sinus (SSS)-stimulated field responses recorded in the nucleus trigeminal caudalis, wherein a reduction in the field response indicates effectiveness in treating migraine or a migraine-related disorder.

13. A method of screening for candidate compounds capable of modulating activity of central nervous system-associated KCNQ potassium channel proteins and capable of treating migraine or a migraine-related disorder, comprising:

a) contacting a test compound with a cell or tissue expressing a KCNQ potassium channel protein;

b) selecting as candidate modulating compounds those test compounds that open or activate the KCNQ potassium channel protein; and

c) identifying those opener or activating compounds of (b) that produce a reduction in superior sagittal sinus (SSS)-stimulated field responses recorded in the nucleus trigeminal caudalis, wherein a reduction in the field response indicates effectiveness in treating migraine or a migraine-related disorder.

14. The method according to claim 12 or claim 13, optionally comprising the step of determining whether the test compound attenuates cortical spreading depression.

15. The method according to claim 12 or claim 13, said method comprising high throughput screening technology.

16. The method according to claim 12 or claim 13, wherein the test compounds are small molecules, therapeutics, or drugs.